REMARKS

Claims 1-56 were pending in the application. Claims 8 and 49-56 are withdrawn from consideration as being drawn to a non-elected invention. Claims 3, 5, 6, 10-13, 27-32, 46-47 have been canceled without prejudice. Claims 1-2, 7, 14-15, 24-26, 31-32 and 45 have been amended. Accordingly, upon entry of the amendments presented herein, claims 1-2, 4, 7-9, 14-26, 33-45 and 48-56 will be pending in the application.

No new matter has been added. Support for the amendments to the claims can be found in the claims and throughout the specification as originally filed.

Amendments to and cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and were done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Rejection of Claims 1-4, 8-11, 15-17, 21-24, 28-29, 31-36, 40-45 and 48-51

Under 35 U.S.C. 112, Second Paragraph

The Examiner has rejected claims 30-31 and 38-40 under 35 U.S.C. 112, second paragraph as being indefinite for reciting the limitation of "said cell" or "the cells." Specifically, the Examiner alleges that there is insufficient antecedent basis in claim 26, from which these claims depend, for this limitation in the claims.

Claims 30 and 31 have been canceled, thereby rendering the rejection moot as it pertains to this claim. With respect to the remaining claims, Applicants respectfully traverse with the Examiner's rejection on the grounds that the claims are clear and definite. Applicants respectfully point out that claim 26 recites the phrase "contacting a cell population with a test agent, said population comprising ***a cell*** having a cholinergic pathway and ***a cell*** having an insulin signaling pathway." Accordingly, there is sufficient antecedent basis in claim 26 for recitation of the phrase "wherein ***the cells*** are mammalian cells," "...human cells" or "...are derived from a nematode," as recited in claims 38-40, respectively. Accordingly, Applicants submit that the rejection of claims 38-40 as being indefinite is improper and respectfully request that the rejection be reconsidered and withdrawn.

Rejection of Claims 1-4, 7, 9-26, 28 and 30-48
Under 35 U.S.C. 112, First Paragraph, Enablement

The Examiner has rejected claims 1-4, 7, 9-26, 28 and 30-48 under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement. Specifically, the Examiner is of the opinion that "[t]he specification, while being enabling for contacting organisms or cells with candidate compounds, does not reasonably provide enablement for all deregulated neurotransmitter pathways as broadly claimed, or for all detectable phenotypes, or for identification of agents capable of enhancing longevity." The Examiner concludes that "given the breadth of the claims, the complex nature of the invention, the state of the art and the few working examples in the specification, it would take an undue amount of experimentation in order for the artisan of ordinary skill to practice the invention commensurate in scope with the claims."

Claims 3, 10-13, 28, 30 and 46-47 have been canceled, thereby rendering this rejection moot as it pertains to these claims. With respect to the remaining claims, Applicants respectfully traverse this rejection for the following reasons.

Section 112 does not require that Applicants describe every equivalent within the scope of the claims so long as the specification provides sufficient teachings for a person of skill in the art to identify additional equivalents ***without undue experimentation*** (In re Wands 8 USPQ2d 1400-1407, 1404 (CAFC, 1988)). The fact that some experimentation is required does not preclude a finding of enablement. See, *e.g.*, In re Angstadt, 537 F.2d 498, 503 and Amgen Inc. v. Chugai Pharmaceutical Co., Ltd., 927 F.2d 1200, 1213 (CAFC 1991). Moreover, "as long as the specification discloses ***at least one method*** for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of §112 is satisfied." In re Fischer, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (emphasis added).

Applicants respectfully submit that based on the teachings in Applicants' specification as well as the general knowledge in the art, one of skill in the art would be able to make and use the claimed invention using only routine experimentation.

A. Deregulated neurotransmitter pathways

The Examiner has alleged that the specification "does not reasonably provide enablement for all deregulated neurotransmitter pathways as broadly claimed." Specifically, the Examiner asserts that "many pathways have nothing to do with longevity," and further asserts that "[f]ew of the claims under examination are limited to those neurotransmitter pathways which are known to be involved in extending longevity in nematodes."

Claims 3, 10-13, 28, 30 and 46-47 have been canceled, thereby rendering this rejection moot as it pertains to these claims. With respect to the remaining claims, Applicants respectfully traverse this rejection. However, in the interest of expediting prosecution, and in no way acquiescing to the validity of the Examiner's rejection, the remaining claims have been amended so as to be directed to methods of identifying an agent capable of enhancing longevity comprising contacting an organism having a deregulated ***cholinergic pathway***, or comprising contacting an organism, cell, cell population or assay composition having a ***cholinergic pathway***." Applicants respectfully submit that the instant specification provides working examples demonstrating that the cholinergic pathway is involved in extending longevity in *C. elegans* (see, e.g., Example 1 at pages 46-47, Example 3 at page 48, Example 5 at pages 50-52 and Example 8 at page 55 of the specification). The specification teaches the genes involved in the cholinergic pathway in *C. elegans* and that these genes are conserved in mammals (see, *e.g.*, page 17, line 15 through page 18, line 2 of the specification). The specification provides guidance in the preparation of mutants having a deregulated cholinergic pathway in *C. elegans* (see, e.g., pages 44-45 of the specification) and in other species (see, e.g., page 36, line 29 thorugh page 37, line 2 and page 37, lines 24-28). The specification also teaches indicators of the cholinergic pathway (see, e.g., pages 19-33 of the specification). Thus, given the extensive teachings in the specification and working examples provided by Applicants, one of ordinary skill in the art could practice the claimed methods of identifying an agent capable of enhancing longevity, wherein the agent is identified based on the ability to inhibit the cholinergic pathway e.g., the activity or expression of a cholinergic pathway molecule, without undue experimentation.

B. Detectable phenotypes

The Examiner has alleged that the specification "does not reasonably provide enablement for all detectable phenotypes." Specifically, the Examiner states that "[a] phenotype could be

anything, as long as it is measurable," that "[m]any phenotypes associated with neurotransmitter pathways have nothing whatsoever to do with longevity," and that "[f]inding modulators of phenotypes other than longevity would not be expected to identify agents which are longevity enhancers."

Claims 3 and 10-13 have been canceled, thereby rendering this rejection moot as it pertains to these claims. With respect to the remaining claims reciting the term "phenotype," Applicants respectfully traverse this rejection. However, in the interest of expediting prosecution, and in no way acquiescing to the validity of the Examiner's rejection, claim1, and the claims which depend therefrom, have been amended so as to be directed to a "method of identifying an agent capable of enhancing longevity comprising contacting an organism having a deregulated cholinergic pathway with a test agent, wherein ***increased lifespan*** is associated with said deregulated cholinergic pathway, assaying for the ability of the test agent to effect said ***increased lifespan***, wherein the agent is identified based on it s ability to enhance said ***increased lifespan*** compared to a suitable control."

Applicants respectfully submit that the instant specification provides extensive teachings regarding increased lifespan as a detectable phenotype in the claimed methods. For example, the specification teaches screening assays in whole organisms (see, *e.g.*, pages 19-24 of the specification) and, in particular, describes assays for measuring life span in *C. elegans* (see, *e.g.*, page 21, lines 12-15). Further, the specification provides working examples in which lifespan assays were carried out in *C. elegans* mutants, *e.g.*, mutants in the cholinergic pathway, (see, e.g., Examples 1-9 at pages 46-52 of the specification) and which demonstrate that mutations in the cholinergic pathway extend lifespan in *C. elegans*. Moreover, lifespan assays in *C. elegans* and other species were commonly known in the art at the time the instant application was filed. Thus, given the extensive teachings in the specification and working examples provided by Applicants, together with the common knowledge in the art, one of ordinary skill in the art could practice the claimed methods involving contacting an organism having a deregulated cholinergic pathway with a test agent, wherein increased lifespan is associated with the deregulated cholinergic pathway, and assaying for the ability of the test agent to effect the increased lifespan, without undue experimentation.

C. Identification of agents capable of enhancing longevity

The Examiner has alleged that the specification "does not reasonably provide enablement for... the identification of agents capable of enhancing longevity." In particular, the Examiner states that "[w]ith the exception of claims 21-23 and 40, which are limited to nematodes, the claims read on all species." The Examiner continues that

> [t]he specification presents data obtained from the nematode *C. elegans*, but presents no data from humans or any other mammals. While the role of insulin signaling pathways in the aging of *C. elegans* was well-understood at the time of the invention... the art cautions that the findings obtained in this species are not easily extendable to mammals or other tetrapods. See for example Tatar (2003) Science 299:1346-1351, who teaches that over the course of evolution there have been significant duplications of genes and changes in physiology which make it difficult to extend the findings on extensions of longevity of any one species to all species in general. While the action of insulin and IGF proteins may be local in flies and worms, it is systemic in mammals and other tetrapods (p. 1350). Tatar teaches that considerable further research is needed to find aging-related targets of insulin and the insulin pathway in tetrapods... As...the art teaches that the findings obtained in *C. elegans* cannot be extended to mammals without considerable additional research, it would take undue experimentation to practice the invention for the scope of any animal beyond nematodes.

Claims 3, 10-13, 28, 30 and 46-47 have been canceled, thereby rendering this rejection moot as it pertains to these claims. With respect to the remaining claims, Applicants respectfully traverse this rejection.

Contrary to the Examiner's assertions, the findings obtained in *C. elegans* regarding the role of insulin signaling pathways in aging in *C. elegans* have been extended to numerous other species. The instant specification teaches that "the influence of the insulin/IGF signaling pathway on lifespan has been conserved across large evolutionary distances," including, for example, in Drosophila (see, *e.g.*, page 15, lines 19-23 of the specification). Further, Applicants respectfully refer the Examiner to Bluher *et al.* 2003 Science 299; 572-574; Al-Regaiey *et al.* 2005 Endocrinology 146(2):851-860; Kloting and Bluher 2005 Experimental Gerontology 40:878-883; and Barbieri *et al.* 2003 Am. J. Physiol. Endocrinol Metab. 285:E10640E1071 (attached hereto as Appendices A, B, C, and E, respectively), publications which collectively teach that insulin signaling plays a role in regulating lifespan across a broad range of species, including yeast, fruit flies and rodents.

Further, Applicants submit that one of ordinary skill in the art, based on the teachings in the specification combined with the common knowledge in the art and the high level of skill in

the art, could practice the claimed methods in species without undue experimentation. The presently pending claims require the steps of (i) contacting a test agent with an organism having a deregulated cholinergic pathway, an organism having a cholinergic pathway, cells having a cholinergic pathway, or an assay composition comprising a cholinergic pathway molecule; (ii) monitoring an indicator of the cholinergic pathway; and (iii) selecting an agent that inhibits the cholinergic pathway. The specification teaches the genes involved in the cholinergic pathway in *C. elegans* and that these genes are conserved in mammals (see, *e.g.*, page 17, line 15 through page 18, line 2 of the specification). Moreover, genes involved in the cholinergic pathway in other species, *e.g*, mammalian species, were common knowledge in the art at the time the instant application was filed. The specification teaches the preparation of mutants having a deregulated cholinergic pathway in *C. elegans* (see, e.g., pages 44-45 of the specification) and in other species (see, e.g., page 36, line 29 through page 37, line 2 and page 37, lines 24-28). In addition, the art is replete with examples of methods for preparing organisms having a deregulated or inactivated gene. The specification also teaches test agents suitable for use in the claimed methods (see, *e.g.,* pages 33-34). Further, methods of contacting cells with test agents, *e.g.*, by *in vitro* or by *in vivo* administration, were well known at the time the instant application was filed. The specification provides extensive guidance for carrying out the screening assays and, in particular, for the selection of an agent that inhibits the cholinergic pathway (*e.g.*, teaching appropriate indicators of the cholinergic pathway), in organisms (see, *e.g*, pages 19-24), in cells (see, *e.g.*, pages 24-29), and in assay compositions (see, *e.g.*, pages 29-33). Finally, the instant specification provides working examples demonstrating that the cholinergic pathway is involved in extending longevity in *C. elegans* (see, e.g., Example 1 at pages 46-47, Example 3 at page 48, Example 5 at pages 50-52 and Example 8 at page 55 of the specification). Thus, given the extensive teachings in the specification and working examples provided by Applicants, together with the common knowledge in the art and high level of skill in the art, one of ordinary skill in the art could practice the claimed methods without undue experimentation.

The Examiner further alleges that the claims as written would not reasonably be expected to identify agents which are enhancers of longevity. The Examiner continues that "[f]or example, claim 1 requires contacting an organism with a test agent, wherein the organism has a deregulated neurotransmitter signaling pathway, measuring a phenotype 'associated with' the

pathway, and concluding that an agent which modulates the phenotype is a longevity-enhancing agent." The Examiner cites Bymaster (2003 European Journal of Neuroscience 17:1403-1410) as teaching that administering the ***muscarinic agonist***, pilocarpine, to wild type mice or mice with deletions of any one of the muscarinic receptors M2-M5 results in death of the mice. The Examiner continues that "rather than identifying pilocarpine as a longevity-enhancing agent, as directed by the claims, the reference correctly teaches that this substance is toxic." The Examiner concludes that "as the claimed methods will identify toxic molecules, the artisan would have to determine how to modify the methods such that longevity-enhancing molecules will instead by identified." Applicants respectfully submit that claim 1, and the claims which depend therefrom, have been amended such that the claims require contacting an organism having a ***deregulated cholinergic pathway*** with a test agent and monitoring the effect of the agent on ***increased lifespan associated with the deregulated cholinergic pathway***. Accordingly, one of ordinary skill in the art would reasonably expect that the claimed methods will necessarily identify agents capable of enhancing longevity, since the methods require that an agent identified by the methods further increases the increased lifespan associated with the deregulated cholinergic pathway in the organism. Moreover, the remaining claims have been amended so that they require contacting an organism, cell, cell population or assay composition with at test agent, and identifying the agent capable of enhancing longevity based on the ability to ***inhibit*** the cholinergic pathway or to ***inhibit*** activity or expression of the cholinergic pathway molecule. The instant specification teaches that a ***deregulated cholinergic pathway***, *e.g.*, mutations in the cholinergic pathway, results in ***increased lifespan*** in *C. elegans*. Accordingly, one of ordinary skill in the art would reasonably expect that the presently claimed methods will identify agents capable of enhancing longevity, since the methods require that an agent identified by the methods inhibits the cholinergic pathway.

Finally, the Examiner alleges that "many of the dependent claims recite mutually exclusive limitations, such that if one were in fact enabled the other would necessarily not be enabled." Applicants respectfully submit that the claims have been amended such that they are directed to methods of identifying an agent capable of enhancing longevity, wherein the agent is is identified based on its ability to ***inhibit*** the cholinergic pathway.

In summary, Applicants respectfully submit that, in view of the ample teachings provided in the specification and the extensive knowledge available in the art, a person of ordinary skill in the art would be able to make and use the claimed methods using only routine experimentation. Accordingly, Applicants respectfully request that the rejection of claims 1-4, 7, 9-26, 28 and 30-48 under 35 U.S.C. 112, first paragraph, for lack of enablement be reconsidered and withdrawn.

Rejection of Claims 1, 3-4, 14-16, 24-26, 28, 30, 33, 38, 41-43, 45 and 47 Under 35 U.S.C. § 102(b)

The Examiner has rejected claims 1, 3-4, 14-16, 24-26, 28, 30, 33, 38, 41-43, 45 and 47 under 35 U.S.C. § 102(b) as being anticipated by Gomeza *et al.* (2001 Life Sciences 68:2457-2466). The Examiner relies on Gomeza *et al.* for teaching "administering oxotremorine to mice with wild-type and mutated muscarinic receptors" and "measuring a phenotype associated with the receptor, namely tail-flick and hot plate test responses and comparing to suitable controls." Based on the foregoing, the Examiner concludes that Gomeza *et al.* anticipates the pending claims.

Claims 3, 10-13, 28, 30 and 46-47 have been canceled, thereby rendering this rejection moot as it pertains to these claims. With respect to the remaining claims, Applicants respectfully traverse this rejection on the grounds that Gomeza *et al.* fails to teach or suggest each and every element of the claimed invention in accordance with 35 U.S.C. §102(b). For a prior art reference to anticipate a claimed invention under 35 U.S.C. 102, the prior art must teach *each and every element* of the claimed invention. *Lewmar Marine v. Barient*, 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987).

The claims are directed to method for identifying an agent capable of enhancing longevity, comprising: contacting an organism having a ***deregulated cholinergic pathway*** with a test agent, wherein increased lifespan is associated with said deregulated cholinergic pathway; assaying for the ability of the test agent to increase the lifespan of the organism as compared to a suitable control, selecting an agent that increases the lifespan, to thereby identify an agent capable of enhancing longevity. The claims are also directed to a method for identifying an agent capable of enhancing longevity, comprising: contacting an organism with a test agent, said

organism having a cholinergic pathway; assaying for the ability of the test agent to inhibit the cholinergic pathway by monitoring the effect of the test agent on one or more of ***the expression, intracellular level, extracellular level, activity, post-translational modification, interaction, cellular localization, or synaptic release of an indicator of said cholinergic pathway*** as compared to a suitable control; and selecting an agent that inhibits the cholinergic pathway; to thereby identify an agent capable of enhancing longevity. The claims are also directed to method for identifying an agent capable of enhancing longevity, comprising: contacting an organism with a test agent, said organism having a cholinergic pathway and an insulin signaling pathway; assaying for the ability of the test agent to inhibit the cholinergic pathway and insulin signaling pathway by monitoring the effect of the test agent on one or more of ***the expression, intracellular level, extracellular level, activity, post-translational modification, interaction, cellular localization, or synaptic release of at least one indicator of said cholinergic pathway*** and insulin signaling pathway; and selecting an agent that inhibits the cholinergic pathway and insulin signaling pathway; to thereby identify an agent capable of enhancing longevity. The claims are still further directed to a method for identifying an agent capable of enhancing longevity, comprising: contacting a cell with a test agent, said cell having a cholinergic pathway; assaying for the ability of the test agent to inhibit the cholinergic pathway by monitoring the effect of the test agent on one or more of ***the expression, intracellular level, extracellular level, activity, post-translational modification, interaction, cellular localization, or synaptic release of an indicator of said cholinergic pathway***; and selecting an agent that inhibits the cholinergic pathway; to thereby identify an agent capable of enhancing longevity. The claims are further directed to a method for identifying an agent capable of enhancing longevity, comprising: contacting a cell with a test agent, said cell having a cholinergic pathway and an insulin signaling pathway; assaying for the ability of the test agent to inhibit the cholinergic pathway and insulin signaling pathway by monitoring the effect of the test agent on one or more of ***the expression, intracellular level, extracellular level, activity, post-translational modification, interaction, cellular localization, or synaptic release of an indicator of said cholinergic pathway*** and insulin signaling pathway; and selecting an agent that inhibits the cholinergic pathway and insulin signaling pathway; to thereby identify an agent capable of enhancing longevity. The claims are also directed to a method for identifying an agent capable of enhancing longevity, comprising: contacting a cell population with a test agent, said population comprising a cell having a cholinergic pathway and a cell having an insulin signaling pathway;

assaying for the ability of the test agent to inhibit the cholinergic pathway and insulin signaling pathway by monitoring the effect of the test agent on one or more of ***the expression, intracellular level, extracellular level, activity, post-translational modification, interaction, cellular localization, or synaptic release of an indicator of the cholinergic pathway*** and insulin signaling pathway; and selecting an agent that inhibits the cholinergic pathway and insulin signaling pathway; to thereby identify an agent capable of enhancing longevity. The claims are yet further directed to a method for identifying an agent capable of enhancing longevity, comprising: contacting ***an assay composition*** with a test agent in vitro, wherein said assay composition comprises a cholinergic pathway molecule; assaying for the ability of the test agent to affect ***the activity or expression of said cholinergic pathway molecule***; selecting an agent that inhibits the activity or expression of said cholinergic pathway molecule; to thereby identify an agent capable of enhancing longevity.

The teachings of Gomeza *et al.* are generally directed to the elucidation of the physiological roles of the muscarinic receptors, M2 and M4 (two of the five known muscarinic receptors), in mice. In particular, Gomeza *et al.* describe the administration of a ***known agonist of muscarinic receptors***, oxotremorine, to wild type mice or mutant mice in which the M2 and/or M4 receptor genes were disrupted. Gomeza *et al.* teach that oxotremorine was previously known to induce analgesia in wild type mice. Gomeza *et al.* monitor the analgesic activity of oxotremorine on the mice by using the ***tail-flick and hot plate tests***, tests that assess pain sensitivity at the spinal and supraspinal level, respectively. Gomeza *et al.* report that oxotremorine caused analgesia in wild type mice and mice lacking the M4 receptor, but failed to cause analgesia in mice lacking the M2 receptor, and conclude that the M2 receptor is involved in mediating the muscarinic effect of analgesia.

Applicants respectfully submit that Gomeza *et al.* fail to teach ***any connection*** between a deregulated cholinergic pathway and ***increased lifespan***. In particular, Gomeza *et al.* fail to teach monitoring ***increased lifespan*** in an organism having a deregulated cholinergic pathway, as required by claims 1-2, 4, 7 and 9. Further, Gomeza *et al.* fail to teach contacting an organism, cell, cell population or assay composition with an agent, wherein an agent capable of enhancing longevity is identified, *e.g.*, ***selected, based on its ability to inhibit the cholinergic pathway*** or to ***inhibit the activity or expression of a cholinergic pathway molecule***, as required by claims 14-26, 31-45 and 48. Gomeza *et al.* only teach the administration of an ***agent known to be an agonist*** of muscarinic receptors, *i.e.*, to ***enhance*** the cholinergic pathway, and fail to

teach ***any selection*** of an agent, let alone the selection of an agent based on the ability to ***inhibit*** the cholinergic pathway or activity or expression of a cholinergic pathway molecule. Indeed, Gomeza fail to disclose ***any agent*** that ***inhibits*** the cholinergic pathway. Moreover, Gomeza et al. fail to teach a method of contacting an assay composition comprising a cholinergic pathway molecule with a test agent ***in vitro***, as required by claims 45 and 48.

In summary, it is evident that Gomeza *et al.* fails to teach each and every element of the claims, and therefore, fails to anticipate the claimed invention. Accordingly, Applicants respectfully request that the rejection of claims 1, 3-4, 14-16, 24-26, 28, 30, 33, 38, 41-43, 45 and 47 under 35 U.S.C. § 102(b) over Gomeza *et al.* be reconsidered and withdrawn.

Rejection of Claims 14-18, 21-22, 24-26, 28, 30, 40-43 and 45-46 Under 35 U.S.C. § 102(b)

The Examiner has rejected claims 14-18, 21-22, 24-26, 28, 30, 40-43 and 45-46 under 35 U.S.C. § 102(b) as being anticipated by Ruvkun (U.S. Patent Application No. 2001/0029617). The Examiner relies on Ruvkun for teaching "contacting organisms with test agents, assaying for the ability of the agent to affect an indicator of the pathway, and identifying said agents as longevity-enhancers," that "the assays be performed on worms" or "*C. elegans* nematodes" and for teaching "measuring phenotypes such as DAF-2 activity." The Examiner further relies on Ruvkun for teaching that "reporter genes can be used" in the assays described, for teaching "measurement of expression and activity of reporters" and that "GFP in particular can be used to determine subcellular localization of the labeled protein." The Examiner further relies on Ruvkun for teaching "contacting nematodes with muscarinic agonists and measuring dauer recovery" and "contacting nematodes with test compounds and detecting the activity or expression of the appropriate neurotransmitter signaling pathway." Based on the foregoing, the Examiner concludes that Ruvkun anticipates the pending claims.

Claims 3, 10-13, 28, 30 and 46-47 have been canceled, thereby rendering this rejection moot as it pertains to these claims. With respect to the remaining claims, Applicants respectfully traverse this rejection on the grounds that Ruvkun fails to teach or suggest each and every element of the claimed invention in accordance with 35 U.S.C. §102(b). For a prior art reference to anticipate a claimed invention under 35 U.S.C. 102, the prior art must teach *each and every*

element of the claimed invention. *Lewmar Marine v. Barient*, 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987).

The teachings of Ruvkun with respect to screening assays for identifying a therapeutic agents, *e.g.*, agents useful as "drugs for the treatment of impaired glucose tolerance conditions, such as diabetes and obesity," are limited to the identification of ***modulators of the insulin signaling pathway*** (see, e.g., paragraphs 0368, 0370, 0416-0422). Further, the teachings of Ruvkun with respect to screening assays for identifying agents that are useful in extending lifespan are similarly limited to the identification of agents that ***modulate the insulin signaling pathway*** (see, e.g., paragraphs 0443-0445). The teachings of Ruvkun related to the cholinergic pathway and, in particular, to the muscarinic receptor, are limited to experiments involving contacting *C. elegans* with a known agonist of the muscarinic receptor and monitoring the single readout of ***dauer formation***. The reference does not teach screening assays for identification of modulators of the cholinergic pathway. In particular, Ruvkun fail to teach or suggest assaying the ability of an agent to inhibit the cholinergic pathway by monitoring the effect of the test agent on one or more of the ***expression, intracellular level, extracellular level, activity, post-translational modification, interaction, cellular localization, or synaptic release of an indicator of the cholinergic pathway,*** as required by the pending claims. Moreover, Ruvkun teach the administration of ***known agonists*** of muscarinic receptors and the effects of those agents on ***dauer recovery***. Ruvkun fail to teach the selection of an agent based on the ability to ***inhibit*** the cholinergic pathway or the activity or expression of a cholinergic pathway molecule. Moreover, Further, Ruvkun fail to teach a method of contacting an assay composition comprising a cholinergic pathway molecule with a test agent ***in vitro***, as required by claims 45 and 48.

In summary, it is evident that Ruvkun fails to teach each and every element of the claims, and therefore, fails to anticipate the claimed invention. Accordingly, Applicants respectfully request that the rejection of claims 14-18, 21-22, 24-26, 28, 30, 40-43 and 45-46 under 35 U.S.C. § 102(b) over Ruvkun be reconsidered and withdrawn.

Rejection of Claims 14-18, 21-26, 28, 30, 40-43 and 45-46 Under 35 U.S.C. § 103(a)

The Examiner has rejected claims 14-18, 21-26, 28, 30, 40-43 and 45-46 under 35 U.S.C. § 103(a) as being obvious over Ruvkun. The Examiner relies on Rubkun for the reasons discussed above. The Examiner acknowledges that "Ruvkun does not teach performing the screening assay for identifying agents which *enhance longevity* as recited in claims 1, 14 and 15, in a parasitic nematode."

Claims 28 and 46 have been canceled, thereby rendering this rejection moot as it pertains to these claims. With respect to the remaining claims, Applicants respectfully traverse this rejection on the grounds that the claimed methods would not have been obvious to one of ordinary skill in the art based on the teachings of Ruvkun.

To establish a *prima facie* case of obviousness, it is necessary for the Examiner to present evidence, preferably in the form of some teaching, suggestion, incentive or inference in the applied references, or in the form of generally available knowledge, that one having ordinary skill in the art would have been motivated to make the claimed invention and would have had a reasonable expectation of success in making the claimed invention. Under section 103, "[b]oth the suggestion and the expectation of success must be founded in the prior art, not in applicant's disclosure" (*Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.* 927 F.2d 1200, 1207, 18 USPQ2d 1016 (Fed. Cir. 1991), quoting *In re Dow Chemical Co.,* 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed Cir. 1988)). Moreover, when considering prior art disclosing a range which "touches" the claimed range, "unexpected results [within the claimed narrow range] may... render the claims unobvious" (see M.P.E.P. § 2131.03).

As discussed above with respect to the rejection of claims 15-24 under 35 U.S.C. 102(b), the teachings of Ruvkun with respect to screening assays for therapeutic agents are limited to the identification of modulators of the insulin signaling pathway. The teachings of Ruvkun related to the cholinergic pathway and, in particular, to the muscarinic receptor, are limited to experiments involving contacting *C. elegans* with an agonist of the muscarinic receptor and monitoring the single readout of ***dauer formation***. Ruvkun fail to teach or suggest assaying the ability of an agent to inhibit the cholinergic pathway by monitoring the effect of the test agent on one or more of the ***expression, intracellular level, extracellular level, activity, post-***

translational modification, interaction, cellular localization, or synaptic release of an indicator of the cholinergic pathway, as required by the pending claims. Moreover, Ruvkun teach the administration of ***known agonists*** of muscarinic receptors and the effects of those agents on dauer recovery. Ruvkun fail to teach ***the selection of an agent*** based on the ability to inhibit the cholinergic pathway or the activity or expression of a cholinergic pathway molecule. Moreover, Further, Ruvkun fail to teach a method of contacting an assay composition comprising a cholinergic pathway molecule with a test agent ***in vitro***, as required by claims 45 and 48.

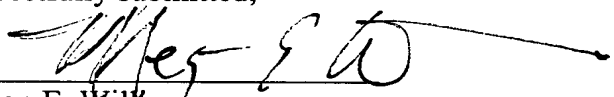
Moreover, one of skill in the art would not have been motivated, based on the disclosure of Ruvkun, to practice the claimed invention. Absent the teachings of the present invention which clearly link the inhibition of the cholinergic pathway with increased life span, one would not have been motivated to modify the teachings of the reference to arrive at the presently claimed assays. Moreover, absent Applicant's teachings there would have been no reasonable expectation of success in identifying agents that increase longevity using such assays.

In summary, Applicants respectfully submit that, in view of the foregoing, it is evident that Ruvkun fails to render the claimed invention obvious. Accordingly, Applicants respectfully request that the rejection of claims 14-18, 21-26, 28, 30, 40-43 and 45-46 under 35 U.S.C. 103(a) be reconsidered and withdrawn.

Applicant believes no additional fees are due with this statement. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. UMY-035 from which the undersigned is authorized to draw.

Dated: May 7, 2007

Respectfully submitted,

By 

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